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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/903,376	07/10/2001	Thomas J. Brennan	R-599	8327

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DELTAGEN, INC.
1031 Bing Street
San Carlos, CA 94070

EXAMINER	
PARAS JR, PETER	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 05/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/903,376	BRENNAN, THOMAS J.	
	Examiner	Art Unit	
	Peter Paras, Jr.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 2/2404.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 28-31 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 28-31 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Applicant's amendment received on 2/24/04 has been entered. Claims 1-27 have been cancelled. New claims 28-31 have been added. Claims 28-31 are pending and are under current consideration.

Sequence Compliance

It is acknowledged that it appears that Applicants have submitted a substitute Figure 2A as such has been referenced in the amendment of 2/24/04. However, the substitute Figure 2A cannot be located and is not part of the file. Accordingly, the instant application is not in sequence compliance as set forth in the Office action mailed on 8/20/03. Applicants are requested to resubmit a substitute Figure 2A to comply with the sequence rules. The Examiner regrets any inconvenience to Applicants.

Upon further consideration the following new grounds of rejection are necessary:

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 28-31 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

The claims are directed to a transgenic mouse embryo whose genome comprises a homozygous disruption in an endogenous 5-HT-2B gene, wherein the

embryo exhibits a developmental abnormality before embryonic day 8.5. The claims are further directed to a method of producing the same mouse.

The instant specification has contemplated that the nucleotide sequence set forth in SEQ ID NO: 1 encodes a 5-HT-2B. The instant specification has further contemplated that disruption of the nucleotide sequence set forth in SEQ ID NO: 1 in a mouse will produce a phenotype related to 5-HT-2B. The instant specification has purported that such mice may be used to identify agents that modulate or ameliorate a phenotype associated with a disruption in SEQ ID NO: 1.

The instant specification has disclosed a heterozygous transgenic mouse whose genome comprises a disruption in SEQ ID NO: 1 [that does not exhibit a phenotype], wherein a mouse embryo whose genome comprises a homozygous disruption in SEQ ID NO: 1 exhibits embryonic lethality, wherein lethality occurs at E8.5-9.5 and the embryo exhibits retarded growth, retarded development, and arrested development or resorption. The claims embrace such a mouse and a method of making the mouse. The instant specification has discussed that phenotype, such as embryonic lethality exhibited by such a transgenic mouse could correlate to a disease or disorder. However, the evidence of record does not provide a correlation between the observed embryonic lethality and any disease or disorder. Moreover, while the specification has purported that the nucleotide sequence set forth in SEQ ID NO: 1 encodes a 5-HT-2B the evidence of record has failed to provide a correlation between any 5-HT-2B related disease/disorder and embryonic lethality. The specification has provided general

assertions that the claimed transgenic mice may be used to identify agents that affect a phenotype related to the mice.

As such, the asserted utility, for the transgenic mouse embraced by the claims, of screening agents that may affect a phenotype of said mouse as provided by the instant specification and encompassed by the claims, does not appear to be specific and substantial. The asserted utility does not appear specific and substantial to the skilled artisan since the evidence of record has not provided any suggestion of a correlation between any 5-HT-2B, embryonic lethality, and any disease or disorder. Since the evidence of record has not provided a correlation between embryonic lethality and any disease or disorder, the utility of identifying agents that affect embryonic lethality is not apparent. The evidence of record has not provided any other utilities for the transgenic mouse embraced by the claims that are specific, substantial, and credible.

The asserted utility of the transgenic mouse embraced by the claims is based on the expectation that disrupting the nucleotide sequence set forth in SEQ ID NO: 1 would result in a detectable phenotype in the mouse. The phenotype observed in the transgenic mice embraced by the claims is embryonic lethality. While the phenotypes exhibited by the claimed transgenic mouse are contemplated to be associated with a disease, the association of embryonic lethality with any disease has yet to be elucidated. In fact the art suggests that phenotypes, such as embryonic lethality, are greatly influenced by the genetic background of the transgenic knockout mouse. For example, Casademunt et al report (EMBO, 1999, 18(21): 6050-6061) nrif -/- mice exhibit differences in embryonic lethality that appear dependent on the genetic

background of the mouse. In short, transgenic nrif -/- mice in a BL6 background cannot survive past E12 while in an Sv129 background such transgenic mice are viable and healthy to adulthood. See the abstract and throughout the entire document. Furthermore, LeCouter et al (Development, 1998, 125: 4669-4679) observe that a null mutation in a p130 is lethal at E11-13 on a Balb/cJ background but when such a mutation is crossed onto a C57BL/6 background the resulting mice are viable and fertile. See the abstract and throughout the entire document. The instant specification has taught use of ES cells from a 129/Sv+P+Mgf-SLJ/J genetic background to generate chimeric mice, which were then bred onto a C57BL6 genetic background to produce the instantly claimed mice exhibiting embryonic lethality as homozygous embryos. See page 52 of the instant specification.

Therefore, the references suggest a need to provide independent evidence of an association of embryonic lethality with a disease or disorder. However, neither the specification nor any art of record provides evidence of the existence of a correlation between embryonic lethality and a disease or disorder, leaving the skilled artisan to speculate and investigate the uses of the transgenic mouse embraced by the claims. The specification essentially gives an invitation to experiment wherein the artisan is invited to elaborate a functional use for the transgenic mouse embraced by the claims. In light of the above, the skilled artisan would not find the asserted utility of the transgenic mouse embraced by the claims to be specific and substantial.

Claim Rejections - 35 USC § 112, 1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 28-31 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Peter Paras, Jr., whose telephone number is (571) 272-0732. The examiner can normally be reached Monday-Friday from 8:30 to 4:30 (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at 571-272-0804. Papers related to this application may be submitted by facsimile transmission. Papers should be faxed via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Official Fax Center number is (703) 872-9306.

Inquiries of a general nature or relating to the status of the application should be directed to Dianiece Jacobs whose telephone number is (571) 272-0532.

Peter Paras, Jr.

Art Unit 1632

PETER PARAS, JR.
PRIMARY EXAMINER